Online Supplement

Aspiration and severe exacerbations in COPD: a prospective study

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Study design, patients, baseline and follow-up study measurements

Studies were conducted at Monash Lung and Sleep at Monash Medical Centre, a tertiary care hospital in Melbourne, Australia. Community-dwelling patients were identified from a hospital pulmonary function database (≥10 pack-year history of smoking, post-bronchodilator FEV₁/FVC≤0.7 and FEV₁<80% predicted [1]) and invited to participate. They had to have a diagnosis of COPD by a general practitioner or respiratory physician, stable lung disease in the preceding 12 weeks and had to be aged 40-80 years. Participation was restricted to those with no known neurological disease, no significant head or neck surgery impacting swallow, no abnormal cranial nerve function on examination, no history of head or neck cancer and no current smokers. Medication use and relevant health history information including comorbidities associated with COPD were obtained from patient history, hospital medical records and medical practitioners.

Measurements of spirometry, gas transfer, lung volumes by body plethysmography and exhaled nitric oxide (FE_{NO}) (MGC Diagnostics Medisoft® and Aerocrine NIOX NO monitoring systems) were obtained as per American Thoracic Society and European

Respiratory Society guidelines [2-6]. Measurements were made at baseline and repeated after 6 months. Patients were instructed to withhold inhaled medications prior to assessments.

Transcutaneous oximetry (NellcorTM PM10N, Covidien) was used to measure peripheral capillary oxygen saturation (S_pO_2). Readings were performed at rest and 5 minutes. Respiratory rate was recorded at rest and one minute after drinking.

The Airways Questionnaire 20 (AQ20), a short version of the St George's Respiratory Questionnaire (SGRQ) [7], was used to evaluate quality of life. It is a validated measure of disease severity and healthcare utilization in COPD [8, 9] with scores \geq 8 predictive of exacerbations [10]. The Eating Assessment Tool-10 (EAT-10) [11] identifies abnormal swallowing symptoms (score of \geq 3) and higher scores (>9) may be predictive of increased risk of aspiration in COPD populations [12]. Patients completed the AQ20 and EAT-10 at baseline, 6 months and 12 months.

Baseline assessments of voice function employing auditory perceptual evaluation and a numerical rating scale (0 = no problem/disruption; 1 = mild disruption to voice production; 2 = moderate with frequent episodes; and 3 = severe voice disruption) were performed. The Oral Health Assessment Tool (OHAT), a valid screening instrument was administered at baseline to identify oral health issues in eight categories: lips, tongue, gums and tissues, saliva, natural teeth, dentures, oral cleanliness and dental pain [13]. Resting pH of unstimulated saliva was also measured as per manufacturer's instructions (GC Australasia Dental) using pH reference ≥6.4 [14].

Table S1. Baseline characteristics of 10 patients who did not complete 12-month follow-up

	Patient characteristics (n=10)	
Age (years, range)	71.0±11.5 (41.2-78.8)	
Gender (M/F)	5/5	
Body Mass Index (kg/m²)	28.6 ± 6.4	
FEV ₁ (% predicted)	48.3±17.4	
FEV ₁ /FVC ratio (%)	50.4±16.3	
TLC (% predicted)	134.6±24.3	
RV/TLC (%)	61.4±8.5	
FE _{NO} (ppb)	31.2±20.7	
$S_{p}O_{2}\left(\% ight)$	93.5±6.6	
Respiratory rate (breaths/min)	20.4±2.5	
Comorbidities (n)		
Cardiovascular disease	9	
Chronic kidney disease	0	
Gastro-oesophageal reflux disease	4	
Obstructive sleep apnoea	1	
Diabetes	0	
Anxiety-depression	3	

Medication (n)

ICS/LABA only	4
ICS/LABA/LAMA	5
Systemic corticosteroids (long term)	2
Antibiotics (long term)	0
Oxygen therapy	3
Influenza vaccination	3
Pneumococcal vaccination	2
Antihypertensives	8
Antianxiety/Antidepressant	4
Angiotensin-converting enzyme inhibitors	1
Reflux medications	4
AQ20 score	10.1±5.6
AQ20 score >8 (n)	6
EAT-10 score	4.1±6.2
OHAT score	2.0 ± 2.4
Resting saliva pH	6.4±0.5

Data shown as mean \pm SD unless otherwise indicated; LABA, long-acting beta agonists; LAMA, long-acting, muscarinic antagonist; ICS, inhaled corticosteroids; AQ20, Airways Questionnaire-20; EAT-10, Eating Assessment Tool; OHAT, Oral Health Assessment Tool.

Table S2. Subgroup analyses of history and types of AECOPD associated with aspiration or no aspiration in 151 patients

	Aspiration not detected $(n = 121)$	Aspiration† detected $(n = 30)$	Odds Ratio (95% CI)	P Value
All exacerbations previous year ≥1; n (%)	42 (34.7)	13 (43.3)	1.44 (0.64-3.24)	0.402
Hospital/ED exacerbations (severe) previous year ≥1; n (%)	24 (19.8)	11 (36.7)	2.34 (0.98-5.57)	0.057
All moderate/severe exacerbations current study; n (%)	88 (72.7)	24 (80)	1.5 (0.56-4.00)	0.491
Hospital/ED exacerbations current study; n (%)	22 (18.2)	15 (50)	4.5 (1.92-10.55)	0.001
Hospital/ED exacerbations ≥2 current study; n (%)	13 (10.7)	6 (20)	2.08 (0.72-6.02)	0.216

[†]Aspiration score of 6-8 on the penetration-aspiration scale [15]; ED, Emergency Department; AECOPD, acute exacerbation of COPD

REFERENCES

- 1. Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Chen R, Decramer M, Fabbri LM, Frith P, Halpin DM, Lopez Varela MV, Nishimura M, Roche N, Rodriguez-Roisin R, Sin DD, Singh D, Stockley R, Vestbo J, Wedzicha JA, Agusti A. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. *Am J Respir Crit Care Med* 2017: 195(5): 557-582.
- 2. Dweik RA, Boggs PB, Erzurum SC, Irvin CG, Leigh MW, Lundberg JO, Olin A-C, Plummer AL, Taylor DR, American Thoracic Society Committee on Interpretation of Exhaled Nitric Oxide Levels for Clinical A. An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. *Am J Respir Crit Care Med* 2011: 184(5): 602-615.
- 3. Graham BL, Brusasco V, Burgos F, Cooper BG, Jensen R, Kendrick A, MacIntyre NR, Thompson BR, Wanger J. 2017 ERS/ATS standards for single-breath carbon monoxide uptake in the lung. *Eur Respir J* 2017: 49(1): 1600016.
- 4. Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CPM, Brusasco V, Burgos F, Casaburi R, Coates A, Enright P, Gustafsson P, Hankinson J, Jensen R, McKay R, Miller MR, Navajas D, Pedersen OF, Pellegrino R, Wanger J. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J* 2005: 26(4): 720-735.
- 5. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay

- R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J, Force AET. Standardisation of spirometry. *Eur Respir J* 2005: 26(2): 319-338.
- 6. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, Casaburi R, Crapo R, Enright P, van der Grinten CPM, Gustafsson P, Hankinson J, Jensen R, Johnson D, Macintyre N, McKay R, Miller MR, Navajas D, Pellegrino R, Viegi G. Standardisation of the measurement of lung volumes. *Eur Respir J* 2005: 26(3): 511-522.
- 7. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. *Am Rev Respir Dis* 1992: 145(6): 1321-1327.
- 8. Alemayehu B, Aubert RE, Feifer RA, Paul LD. Comparative Analysis of Two Quality-of-Life Instruments for Patients with Chronic Obstructive Pulmonary Disease. *Value Health* 2002: 5(5): 437-442.
- 9. Quirk FH, Jones PW. Back to basics: How many items can adequately represent health-related quality of life in airways disease? *Eur Respir Rev* 1997: 7(42): 50-52.
- 10. Miravitlles M, García-Sidro P, Fernández-Nistal A, Buendía MJ, Espinosa de Los Monteros MJ, Esquinas C, Molina J. The chronic obstructive pulmonary disease assessment test improves the predictive value of previous exacerbations for poor outcomes in COPD. *Int J Chron Obstruct Pulmon Dis* 2015: 10: 2571-2579.
- 11. Belafsky PC, Mouadeb DA, Rees CJ, Pryor JC, Postma GN, Allen J, Leonard RJ. Validity and reliability of the Eating Assessment Tool (EAT-10). *Ann Otol Rhinol Laryngol* 2008: 117(12): 919-924.

- 12. Regan J, Lawson S, De Aguiar V. The Eating Assessment Tool-10 Predicts Aspiration in Adults with Stable Chronic Obstructive Pulmonary Disease. *Dysphagia* 2017: 32(5): 714-720.
- 13. Chalmers JM, King PL, Spencer AJ, Wright FA, Carter KD. The oral health assessment tool--validity and reliability. *Aust Dent J* 2005: 50(3): 191-199.
- 14. Cunha-Cruz J, Scott J, Rothen M, Mancl L, Lawhorn T, Brossel K, Berg J. Salivary characteristics and dental caries: evidence from general dental practices. *J Am Dent Assoc* (1939) 2013: 144(5): e31-40.
- 15. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. *Dysphagia* 1996: 11(2): 93-98.